Steadman 09/856,050

```
=> d his 1

     (FILE 'HCAPLUS' ENTERED AT 15:24:26 ON 14 OCT 2003)
L22          45 S L4 OR L14 OR L21

=> d que l22 '
L1         1947 SEA FILE=REGISTRY LVHGKL|DDDDK/SQSP
L2         1390 SEA FILE=HCAPLUS L1
L4            1 SEA FILE=HCAPLUS L2 AND NEUROSIN#
L5           72 SEA FILE=HCAPLUS L2 AND CLEAVAGE(3A)SITE#
L8           35 SEA FILE=HCAPLUS L5 AND ENTEROKINASE#
L9           25 SEA FILE=HCAPLUS L2 AND (ENTEROKINASE#(3A)CLEAV?(3A)SITE#)
L10          35 SEA FILE=HCAPLUS L8 OR L9
L11          19 SEA FILE=HCAPLUS L2 AND ((PROTEINASE# OR PROTEASE#)(3A)CLEAV?
                (3A)SITE#)
L13          15 SEA FILE=HCAPLUS L11 AND (SPACER# OR LINKER# OR FUSION)
L14          45 SEA FILE=HCAPLUS L10 OR L13
L15         550 SEA FILE=HCAPLUS UEMURA H?/AU
L16          29 SEA FILE=HCAPLUS OKUI A?/AU
L17         112 SEA FILE=HCAPLUS KOMINAMI K?/AU
L18        1980 SEA FILE=HCAPLUS YAMAGUCHI N?/AU
L19         796 SEA FILE=HCAPLUS MITSUI S?/AU
L20        3411 SEA FILE=HCAPLUS (L15 OR L16 OR L17 OR L18 OR L19)
L21           1 SEA FILE=HCAPLUS L20 AND CLEAVAGE(3A)SITE#
L22          45 SEA FILE=HCAPLUS L4 OR L14 OR L21


=> d ibib abs l22 1-45

L22  ANSWER 1 OF 45  HCAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:         2003:656931  HCAPLUS
DOCUMENT NUMBER:          139:207750
TITLE:                    Soluble fusion proteins of immunoglobulins
                          and ligands for tumor necrosis factor receptors for
                          therapeutic use
INVENTOR(S):              Gaide, Oliver; Schneider, Pascal; Tschopp, Juerg
PATENT ASSIGNEE(S):       Apoxis S.A., Switz.
SOURCE:                   PCT Int. Appl., 51 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 German
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     WO 2003068977      A2   20030821       WO 2002-EP9354   20020821
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD,
             RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
             CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
             PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
             NE, SN, TD, TG
     DE 10205583        A1   20030821       DE 2002-10205583 20020211
```

Search completed by David Schreiber 308-4292

PRIORITY APPLN. INFO.: DE 2002-10205368 A 20020210
DE 2002-10205583 A 20020211

AB **Fusion** proteins with an N-terminal domain of the the Fc region of an Ig and a C-terminal extracellular domain of a ligand for a tumor necrosis factor receptor ligand connected by a flexible **linker** containing a **proteinase cleavage site** are described for use in the therapeutic induction of apoptosis. These proteins lack the membrane domain of a ligand such as Fas-L and so are soluble and useful as therapeutics. These **fusion** proteins are particularly useful for in utero treatment as the uterus does not carry Ig receptors. **Fusion** proteins of Fc and the extracellular domain of ectodysplasin-A were administered i.v. to pregnant female tabby mice, which carry a defect in the ectodysplasin-A gene. The treatment had no effect on the mothers, but the offspring showed reversion of the tabby phenotype with normal hair and skin development. The reversion was stable.

L22 ANSWER 2 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:656892 HCAPLUS
DOCUMENT NUMBER: 139:202456
TITLE: Chimeric molecules comprising linker with enzyme cleavable **site** for **cleavage** in a treated host
INVENTOR(S): Rutter, William J.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 90 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003068934	A2	20030821	WO 2003-US4482	20030214

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-357740P P 20020214
AB The present invention relates to chimeric mols. containing component mols. that are linked together in a non-naturally occurring manner where the linker contains at least one enzyme **cleavage site**, and the enzyme **cleavage site** is engineered to be cleaved by an enzyme in a treated subject. The present invention also relates to compns. and kits containing the chimeric mols., methods of making the chimeric mols. in a production host, methods of using the present chimeric mols. for diagnostic, prophylactic, therapeutic, and nutritional purposes in subjects requiring such.

L22 ANSWER 3 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:551526 HCAPLUS

DOCUMENT NUMBER: 139:112735
TITLE: Use of Escherichia TolA domain for production and purification of recombinant fusion proteins
INVENTOR(S): Gokce, Isa; Anderluh, Gregor; Lakey, Jeremy Hugh
PATENT ASSIGNEE(S): Newcastle University Ventures Limited, UK
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003057708	A2	20030717	WO 2003-GB78	20030110

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2002-683 A 20020110

AB The present invention relates to fusion proteins, particularly for use in expression and/or purification systems. The present inventors have found that the TolAIII domain has remarkable properties which are of particular use as a fusion protein partner to achieve high levels of expression in a host cell. In one aspect of the invention, a TolAIII domain or a functional homolog, fragment, or derivative thereof is located towards the N-terminus of the fusion polypeptide and a non-TolA polypeptide is located towards the C-terminus of the fusion polypeptide. Thus, numerous proteins were produced with recombinant E. coli as fusions with E. coli TolA domain III, e.g., large amts. of BCL-XL protein were prepared For this purpose, three different expression plasmids were created: pTolE, pTolX, and pTolT. These plasmids are used to produce fusion proteins which may be cleaved with **enterokinase**, factor Xa, or thrombin, resp., to produce the desired protein.

L22 ANSWER 4 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:492554 HCAPLUS
DOCUMENT NUMBER: 139:65404
TITLE: Soluble human acetylglucosamine-1-phosphotransferase containing an artificial proteolytic **cleavage site** to generate α and β subunits
INVENTOR(S): Canfield, William; Kudo, Mariko
PATENT ASSIGNEE(S): Novazyme Pharmaceuticals, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 55 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 2003119088 A1 20030626 US 2001-23888 20011221
WO 2003057826 A2 20030717 WO 2002-US37624 20021220
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2001-23888 A 20011221

AB Recombinant soluble UDP-N-acetylglucosamine:lysosomal enzyme N-acetylglucosamine-1-phosphotransferase (I, EC 2.7.8.17) is not efficiently subject to post-translational proteolytic cleavage when expressed in mammalian cells and uncleaved forms have poor GlcNAc phosphotransferase activity. To solve this problem, the invention shows that by interposing a unique proteolytic **cleavage site** between the α and β subunits in the I polyprotein, the polyprotein is cleaved and when expressed with the γ subunit, effectively phosphorylates an enzyme substrate. In addition, the α and β subunits alone without the γ subunit are catalytically active. Furthermore, the absence of the γ subunit results in loss of substrate specificity to only those lysosomal enzymes targeted via the mannose-6-phosphate targeting systems, e.g., acid α-glucosidase, acid β-galactosidase, β-hexaminidase, and others. This loss of substrate specificity allows the soluble I containing the α and β tetramer to effectively phosphorylate any glycoprotein having an appropriate acceptor oligosaccharide. Patients suffering from a lysosomal storage disease can be treated by contacting a lysosomal hydrolase with soluble I to produce a lysosomal hydrolase with an N-acetylglucosamine-1-phosphate, removing the N-acetylglucosamine by contact of the lysosomal hydrolase with a N-acetylglucosamine-1-phosphodiester-N-acetylglucosaminidase (EC 3.1.4.45) to produce a phosphorylated lysosomal hydrolase, and administering an amount of the phosphorylated enzyme sufficient to treat said disease.

L22 ANSWER 5 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:377136 HCAPLUS
DOCUMENT NUMBER: 138:390403
TITLE: Site-specific tagging of human choriogonadotropin and other proteins with cysteine-containing knobs for protein purification, structure-function probing and mapping the distances between proteins
INVENTOR(S): Moyle, William R.; Xing, Yongna
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003040695	A2	20030515	WO 2002-US35914	20021108

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-345283P P 20011108

AB Compns. containing a knob attached to a specific site of a protein and methods of producing and using these compns. are disclosed. The compns. comprise a knob, a tail portion and a protein portion. The protein portion contains a substituted cysteine residue at the desired location of labeling. The tail portion is located at the terminal end of the protein portion. The knob is linked to the end of the tail portion and contains a cysteine residue. The substituted cysteine residue on the protein portion and the cysteine residue on the knob form a disulfide bond, thereby tagging the protein portion at the desired site with the knob. Methods for attaching knobs to human choriogonadotropin (hCG) at specified sites are disclosed. These methods involve inserting constructs capable of expressing native hCGβ or hCGβ-S138C, and native hCGα or hCGα-cysteine substituted analogs into a cell for co-expression, and fusing a knob to residue 140 or 145 of hCGβ. Methods for using the site specifically modified proteins knobs are disclosed. The protein knobs may be used to map distances between proteins, probe the surface of a protein-protein interface, form a complex between two unrelated proteins, probe the structure and function of the protein knob-protein, to immobilize proteins on surfaces, to deliver proteins to cells, as a targeting protein, and for protein purification

L22 ANSWER 6 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2003:282744 HCAPLUS
DOCUMENT NUMBER: 138:282323
TITLE: High-throughput clonal selection of recombinant CHO cells using a dominant selectable and amplifiable metallothionein-GFP **fusion** protein
INVENTOR(S): Sunstrom, Noelle-anne; Bailey, Charles Geoffrey
PATENT ASSIGNEE(S): Unisearch Limited, Australia
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003029461	A1	20030410	WO 2002-AU1352	20021003

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,

PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: AU 2001-8051 A 20011003

AB The present invention relates to a method of screening cells for an alteration, typically an amplification, in the copy number of a nucleic acid of interest using an amplifiable nucleic acid linked to a reporter nucleic acid; a method of screening cells for increased expression of a polypeptide of interest derived from the nucleic acid of interest; and related cells and genetic constructs. The method allows for high throughput screening of recombinant cells expressing a polypeptide or protein of interest and, in particular, for screening of cells expressing the polypeptide or protein of interest at elevated levels. It has surprisingly been found that an amplifiable nucleic acid linked to a reporter nucleic acid can be used to screen cells having an altered (eg. amplified) copy number of a nucleic acid of interest. This system can also be used to rapidly screen cells for expression of a product of interest and in protocols for high throughput selection of cells producing high levels of a product of interest. In the system exemplified below, selection and amplification can be visually monitored, thus allowing efficient screening of recombinant gene-pos. clones and resulting in selection of clones having a high level of expression of a product of interest following amplification. The representative amplifiable nucleic acid used was the human metallothionein (MT) gene and the reporter nucleic acid chosen was the green fluorescent protein (GFP) gene. The genes were linked by fusing the nucleic acids in frame to allow production of a **fusion** protein, MTGFP (referred to as "the **fusion** marker "). Cells transfected with the MTGFP construct respond to successive stepwise cadmium selection and amplification with increasing fluorescence that can be monitored using a flow cytometer or a fluorometer (a microtiter plate reader equipped with the appropriate filters to measure GFP fluorescence). Expression of MTGFP acted as a dominant selectable marker allowing rapid and more efficient selection of clones at defined metal concns. than with the antibiotic G418. Cells harboring MTGFP responded to increasing metal concns. with a corresponding increase in fluorescence. There was also a corresponding increase in recombinant protein production, indicating that MTGFP could be used as a selectable and amplifiable gene for the coexpression of foreign genes. Using the expression vector encoding MTGFP, the authors demonstrate a high-throughput clonal selection protocol for the rapid isolation of high-producing clones from transfected CHO cells. The authors were able to isolate cell lines reaching specific productivities of >10 μg hGH/106 cells/day within 4 wk of transfection. The advantage of this method is that it can be easily adapted for automated procedures using robotic handling systems.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 7 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2003:173635 HCAPLUS

DOCUMENT NUMBER: 138:216487

TITLE: A method of sequestering a protein in a complex to simplify purification by manufacture as a **fusion** protein with polymerizing protein

INVENTOR(S): Tillett, Daniel; Thomas, Torsten

PATENT ASSIGNEE(S): Protigene Pty. Ltd., Australia

SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003018616	A1	20030306	WO 2002-AU1159	20020827

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: AU 2001-7298 A 20010827

AB A method of manufacturing a protein in an expression host that simplified purification without the need for extensive chromatog. or affinity chromatog. purification is described. The method involves manufacturing the protein as a **fusion** protein with a carrier that forms homopolymers. The protein can be purified by capture with the unmodified form of the homopolymer-forming protein. The **fusion** protein can be hydroyzed with a proteinase specific for a **linker** peptide connecting the two moieties. Methods of using the FtsZ protein of Escherichia coli as the carrier moiety are demonstrated.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 8 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:1234 HCAPLUS
DOCUMENT NUMBER: 138:72000
TITLE: Secretory manufacture of proteins with an N-terminal leader peptide extension using a yeast expression host
INVENTOR(S): Kjeldsen, Thomas Borglum; Balschmidt, Per; Pettersson, Annette Frost; Vad, Knud; Brandt, Jakob; Havelund, Svend
PATENT ASSIGNEE(S): Novo Nordisk A/S, Den.
SOURCE: U.S., 53 pp., Cont.-in-part of U. S. Ser. No. 991,801, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6500645	B1	20021231	US 1999-324217	19990602

PRIORITY APPLN. INFO.:
DK 1994-712 A 19940617
US 1994-286059 B1 19940804
US 1995-490689 B2 19950615
DK 1995-1449 A 19951220
US 1996-766011 B2 19961213
DK 1996-1482 A 19961220
US 1997-991801 B2 19971216

OTHER SOURCE(S): MARPAT 138:72000

AB A method of secretory manufacture of proteins using a yeast host that protects

the N-terminus of the secreted protein from post-processing degradation is described. The protein is synthesized as a precursor with a signal peptide and a leader peptide between the signal peptide and the true N-terminus of the protein. The junction of the two peptides should constitute a **cleavage site** for a processing proteinase such as KEX2. The leader peptide may include sequences with other functions, such as an affinity lable or a glycosylation site. Genes for a series of proinsulin derivs. including a leader peptide were constructed by standard methods. Yields of proteins manufactured in a Saccharomyces host resulted in yields up to 3-fold greater than those from a control gene encoding the proinsulin without a leader peptide. The leader peptides were efficiently released with Achromobacter lyticus protease I. Cleavage could be carried out in vitro or in vivo using a host overexpressing the YAP3 gene for the enzyme. Hosts expressing the YAP3 gene showed a 4-fold increase in yield over those not expressing the gene.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 9 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:965025 HCAPLUS
DOCUMENT NUMBER: 138:35722
TITLE: **Enterokinase** cleavage sequences useful for isolation of fusion proteins
INVENTOR(S): Ley, Arthur Charles; Luneau, Christopher Jon; Ladner, Robert Charles
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 67 pp., Cont.-in-part of U. S. Ser. No. 597,321, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002192789	A1	20021219	US 2001-884767	20010619

PRIORITY APPLN. INFO.: US 2000-597321 B2 20000619
OTHER SOURCE(S): MARPAT 138:35722

AB Novel **enterokinase** cleavage sequences are provided. To identify novel **enterokinase** cleavage sequences, a substrate phage library, having a diversity of about 2 + 108 amino acid sequences, was screened against **enterokinase**. The substrate phage library was design to include a peptide-variegated region in the display polypeptide consisting of 13 consecutive amino acids and allowing any amino acid residue except cysteine to occur at each position. The substrate phage library was also characterized by inclusion of an N-terminal tandem arrangement of a linear and a disulfide-constrained streptavidin recognition sequence. The screen was carried through a total of 5 rounds of increasing stringency to obtain phage that could be released by incubation with recombinant light chain **enterokinase** after binding to immobilized streptavidin. Also disclosed are methods for the rapid isolation of a protein of interest present in a fusion protein construct including a novel **enterokinase** cleavage sequence of the present invention and a ligand recognition sequence for capturing the fusion construct on a solid substrate. Preferred peptides of the present invention (e.g., Asp-Ile-Asn-Asp-Asp-Arg-Xaa) show rates of cleavage (kcat/Km) up to 30-fold that of the known **enterokinase** cleavage substrate (Asp)4-Lys-Ile.

L22 ANSWER 10 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:869214 HCAPLUS
DOCUMENT NUMBER: 137:365964
TITLE: Universal fluorescent sensors using two **linker**-connected fluorescent polypeptides displaying fluorescence resonance energy transfer
INVENTOR(S): Fricker, Mark David; Vaux, David John Talbutt
PATENT ASSIGNEE(S): Isis Innovation Limited, UK
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002090987	A2	20021114	WO 2002-GB2183	20020510
WO 2002090987	A3	20030612		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2001-11459 A 20010510

AB A probe comprises: (1) a target binding site moiety which is attached to a first fluorescent polypeptide; (ii) a mimic moiety which is capable of binding to the target binding site moiety and is attached to a second fluorescent polypeptide; and (iii) a **linker** which connects the two fluorescent polypeptides and which allows the distance between said fluorescent polypeptides to vary, said fluorescent polypeptides being so as to display fluorescence resonance energy transfer (FRET) between them, wherein the **linker** comprises one or more of: (1) a sequence capable of being recognized and bound by an immobilized component; (2) a **protease cleavage site**; (3) a non-analyte binding site; (4) two or more copies of the sequence (SerGly3); or (5) one or more copies of a rod domain from a structural protein. Probes of the invention are used, for example, in the detection of a wide range of substances or in the identification of inhibitors of the interaction between two substances which, in the absence of an inhibitor, interact with each other. Plasmid pTrcCFRET3 was prepared encoding a probe having enhanced cyan fluorescent protein (eCFP), a hexa-histidine tag, an epitope tag, and enhanced yellow fluorescent protein (eYFP).

L22 ANSWER 11 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:784265 HCAPLUS
DOCUMENT NUMBER: 137:306642
TITLE: Activation of recombinant human chymase by baculovirus-insect cell expression as signal peptide fusion and **enterokinase** cleavage
INVENTOR(S): Kaki, Hiroki; Murayama, Shuji; Tatsui, Akira; Miyazaki, Sumio; Takai, Shinji
PATENT ASSIGNEE(S): Katakura Industries Co., Ltd., Japan; Toa Eiyo, Ltd.

SOURCE: Jpn. Kokai Tokkyo Koho, 17 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002300886	A2	20021015	JP 2001-108186	20010406

PRIORITY APPLN. INFO.: JP 2001-108186 20010406

AB Production of thermostable human chymase by recombinant expression of inactive form and activation by **enterokinase** cleavage, is disclosed. The expression of recombinant human chymase was achieved in a baculovirus-insect cell system using a fusion protein construct. The recombinant baculovirus was produced with DNA coding for a prochymase fusion protein inserted immediately downstream of the signal sequence for the secreted protein, 30K protein. In each construct, the natural prepro-peptide sequence of the protease was replaced by the amino acid sequence for the **enterokinase cleavage site** of trypsinogen. Silkworm cells infected with either of the modified baculovirus produced milligram quantities of each fusion protein per L of culture. Treatment of the chymase-fusion protein with **enterokinase** with **enterokinase** produced enzymically active proteases with properties of the native enzymes with regard to substrate specificity and inhibitor profiles. Thermostability, however, was improved.

L22 ANSWER 12 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:688578 HCAPLUS
DOCUMENT NUMBER: 137:211342
TITLE: Drug screening for effectors of G protein αS subunits and β2-adrenoreceptor **fusion** proteins, localized to cell membranes, for signal transduction regulation
INVENTOR(S): Kobilka, Brian; Lee, Tae Weon
PATENT ASSIGNEE(S): The Board of Trustees of the Leland Stanford Junior University, USA
SOURCE: U.S., 38 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6448377	B1	20020910	US 2000-672239	20000927

PRIORITY APPLN. INFO.: US 2000-672239 20000927

AB The present invention provides G protein α-subunit (Gs (adenylate cyclase-stimulating) subunit) **fusion** proteins with β2-adrenoreceptor characterized by constitutive localization to the plasma membrane. These **fusion** proteins show enhanced binding to one or more of the normal receptor binding partners for that α-subunit and efficient binding to and activation of G protein binding partners. The distribution of these modified α-subunits, which are tethered to the plasma membrane, allows the regulation of receptor-G protein coupling, and thus G-protein signaling, in various biol. systems.

Search completed by David Schreiber 308-4292

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 13 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:594989 HCAPLUS
DOCUMENT NUMBER: 137:153954
TITLE: Method for producing pig pancreatic trypsin with yeast
INVENTOR(S): Mueller, Rainer; Glaser, Stephan; Geipel, Frank; Thalhofer, Johann-Peter; Rexer, Bernhard; Schneider, Claus; Ratka, Michael; Ronning, Stephanie; Eckstein, Hellmut; Giessel, Claudia
PATENT ASSIGNEE(S): Roche Diagnostics G.m.b.H., Germany; F. Hoffmann-La Roche A.-G.; et al.
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002061064	A2	20020808	WO 2002-EP1072	20020201

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2001-102342 A 20010201
AB The invention relates to a method for producing, with Pichia pastoris, pig pancreatic trypsin. The recombinant enzyme is soluble in Pichia pastoris and is secreted into the culture medium. Expression at pH 3.0 - 4.0 substantially prevents proteolytic degradation of trypsinogen into inactive peptides. Thus, recombinant Pichia pastoris secreting pig pancreatic trypsin were prepared These yeast were transformed with expression vectors containing a chimeric gene for N-terminal truncated trypsinogen fused to Saccharomyces cerevisiae α-factor signal peptide. The gene was altered to contain yeast-preferred codons. The Pichia AOX1 gene promoter was used to drive expression of the chimeric gene.

L22 ANSWER 14 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:502770 HCAPLUS
DOCUMENT NUMBER: 137:74759
TITLE: Preparation of highly purified mocarhagin and cloning of cDNA encoding it and therapeutics uses of enzyme
INVENTOR(S): Boodhoo, Amechand; Seehra, Jasbir S.; Shaw, Gray; Sako, Dianne
PATENT ASSIGNEE(S): Genetics Institute, Inc., USA
SOURCE: U.S., 38 pp., Cont.-in-part of U.S. Ser. No. 12,637, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2

Search completed by David Schreiber 308-4292

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6413760	B1	20020702	US 1998-26001	19980218
AU 9872525	A1	19981111	AU 1998-72525	19980414
US 2002127691	A1	20020912	US 2001-996620	20011127

PRIORITY APPLN. INFO.: US 1997-843373 B2 19970415
US 1998-12637 B2 19980123
US 1998-26001 A 19980218
WO 1998-US7998 W 19980414

AB Highly purified mocarhagin, a cobra venom protease, is disclosed. Pharmaceutical compns. and therapeutic uses of the highly purified protease are also provided. Polynucleotides encoding such protease and related proteases are also disclosed. Methods of purifying the cobra venom proteinase mocarhagin to near-homogeneity and cloning of a cDNA encoding it are described. The enzyme hydrolyzes a number of proteins involved in cell adhesion and platelet agglutination and may be useful in the treatment of disorders such as restenosis. Crude venom was fractionated by affinity chromatog. against immobilized heparin; by size exclusion chromatog.; and by ion-exchange chromatog. against a Mono-S column. Yield of mocarhagin was 2-3 mg/g venom and purity was >95%. A cDNA was cloned from a N. mossambica mossambica venom gland library by PCR using amino acid sequence-derived probes. The protein was manufactured by expression of a cDNA encoding an analog containing a **cleavage site** for **enterokinase** at the C-terminus of the signal peptide in COS cells. **Enterokinase** cleavage of the precursor to the mature form was demonstrated.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 15 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:350601 HCAPLUS
DOCUMENT NUMBER: 136:364902
TITLE: Large scale production of recombinant peptides by expression as PTH fragment **fusion** protein and protease cleavage
INVENTOR(S): Yamada, Takao; Suenaga, Masato
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 103 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002036762	A1	20020510	WO 2001-JP9476	20011029
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001096023	A5	20020515	AU 2001-96023	20011029

JP 2003079380 A2 20030318 JP 2001-330729 20011029
PRIORITY APPLN. INFO.: JP 2000-331170 A 20001030
JP 2001-195522 A 20010627
WO 2001-JP9476 W 20011029

AB Methods for mass industrial scale recombinant production of peptides with authentic N-termini are provided. The method comprises expressing the peptide as part of a **fusion** protein with PTH N-terminal fragment PTH(1-34) attached via a **linker** containing **protease cleavage site**. **Enterokinase**, factor Xa, or thrombin can be used for protease cleavage. Production of human apelin-36, human G protein-coupled receptor 8 GPR8 ligand, and human G protein-coupled receptor ZAQ ligand is described.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 16 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:131509 HCAPLUS
DOCUMENT NUMBER: 136:195300
TITLE: Genetically modified cells and methods for expressing recombinant human heparanase and methods of its purification
INVENTOR(S): Ayal-Hershkovitz, Maty; Moskowitz, Haim; Miron, Daphna; Gilboa, Ayelet; Mimon, Madelene; Ben-Artzi, Hanna; Yacoby-Zeevi, Oron; Pecker, Iris; Peleg, Yoav; Schlomi, Yinon
PATENT ASSIGNEE(S): Insight Strategy & Marketing Ltd., Israel
SOURCE: U.S., 66 pp., Cont.-in-part of U.S. Ser. No. 71,618, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 17
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6348344	B1	20020219	US 1999-260038	19990302
US 5968822	A	19991019	US 1997-922170	19970902
US 6177545	B1	20010123	US 1998-71739	19980501
CA 2329142	AA	19991111	CA 1999-2329142	19990429
WO 9957244	A1	19991111	WO 1999-US9256	19990429
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9937705	A1	19991123	AU 1999-37705	19990429
EP 1076689	A1	20010221	EP 1999-920135	19990429
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002513560	T2	20020514	JP 2000-547200	19990429
US 6475763	B1	20021105	US 2000-487716	20000119
US 6426209	B1	20020730	US 2000-635923	20000810
NO 2000005100	A	20001228	NO 2000-5100	20001010
US 2003068806	A1	20030410	US 2002-137351	20020503

PRIORITY APPLN. INFO.: US 1997-922170 A2 19970902
US 1998-71618 B2 19980501
US 1998-71739 A2 19980501
US 1999-260038 A 19990302
WO 1999-US9256 W 19990429
US 2000-487716 A1 20000119
US 2000-635923 A1 20000810

AB Bacterial, yeast, and animal cells and methods for overexpressing recombinant heparanase in cellular systems, methods of purifying recombinant heparanase therefrom and modified heparanase species which serve as precursors for generating highly active heparanase by proteolysis are provided. Thus, cloning of human heparanase cDNA into baculovirus-infected High 5 and Sf21 cells yielded 0.44 and 0.16 mg enzyme/mL, resp. Enzyme purification is achieved by cation-exchange chromatog. on Source-S or affinity chromatog. with anti-native heparanase antibodies. Highly active partially proteolytically cleaved forms of heparanase were identified. This led to the construction of recombinant heparanase containing (1) an **enterokinase cleavage site** (Ser-Gln-Val-Asn-Gln) leading to cleavage between residues 119 and 120, or (2) a cathepsin L **cleavage site** leading to **cleavage** between residues 157 and 158.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 17 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:473045 HCAPLUS
DOCUMENT NUMBER: 135:73697
TITLE: A bioluminescence resonance energy transfer (BRET) fusion molecule and method of use
INVENTOR(S): Joly, Erik
PATENT ASSIGNEE(S): Biosignal Packard Inc., Can.
SOURCE: PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001046694	A2	20010628	WO 2000-CA1513	20001222
WO 2001046694	A3	20011129		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: CA 1999-2292036 A 19991222

AB This invention provides a bioluminescence resonance energy transfer (BRET) fusion mol., and method of use. The fusion mol. comprises three components: a bioluminescent donor protein (BDP), a modulator, and a fluorescent acceptor mol. (FAM), wherein the FAM can accept energy from the BDP-generated luminescence when these components are in an appropriate spatial relationship and in the presence of an appropriate substrate. The modulator can either influence the proximity/orientation of the BDP and

the FAM and thereby the energy transfer between these components, or it can play a different role in affecting the energy transfer between the BDP-generated activated product and the FAM. The fusion protein, Rluc:PKA:EYFP (containing Renilla luciferase fusion protein with a synthetic peptide containing a phosphorylation site for protein kinase A fusion protein with enhanced yellow fluorescent protein), was recombinantly prepared and used in a BRET assay with coelenterazine h derivative (as luminescent substrate). The BRET ratio was forskolin dose-dependent such that the BRET ratio decreased with an increase in the concentration of forskolin.

L22 ANSWER 18 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:279733 HCAPLUS
DOCUMENT NUMBER: 134:321574
TITLE: Genetic vector for soluble expression of target protein in E. coli
INVENTOR(S): Duan, Jubao; Zou, Minji; Wang, Jiaxi; Cai, Xin
PATENT ASSIGNEE(S): Inst. of Basic Medical Sciences, Academy of Military Medical Science, PLA, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 16 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1271777	A	20001101	CN 2000-108742	20000602

PRIORITY APPLN. INFO.: CN 2000-108742 20000602

AB The invention relates to genetic vectors to produce soluble recombinant target protein in E. coli. These vectors including pZD1, pZD2, and pZD-IL6 contains a bicistronic gene: one is selected from gene trxA, or genes for protein disulfide-bond isomerase and glutaredoxin; another one is for the target protein. The translational initiation signal SD site (Shine Dalgarno sequence) are placed before the AUG codon for the first gene and between the two genes for the second target gene. The cDNA for **enterokinase cleavage site** is also inerted between the two genes in case of the generation of the fusion protein resulted from translational readthrough. The invention is exemplified by expressing gene for interleukin 6 (IL-6) or IL-6 receptor α in conjunction with trxA gene. Methods of expression and purification of IL-6 or IL-6Rα are described. The target soluble protein can also be insulin, lysozyme, interferon, renin, prolactin, plasminogen activator, human trypsin inhibitor α1, factor VIII, cytokines, cytokine receptors, or their fragments.

L22 ANSWER 19 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:265565 HCAPLUS
DOCUMENT NUMBER: 134:291103
TITLE: Methods of using a Mycobacterium tuberculosis coding sequence in gene and protein fusions to facilitate stable and high yield expression of heterologous proteins
INVENTOR(S): Skeiky, Yasir; Guderian, Jeffrey
PATENT ASSIGNEE(S): Corixa Corporation, USA
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

Search completed by David Schreiber 308-4292

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001025401	A2	20010412	WO 2000-US27652	20001006
WO 2001025401	C2	20020926		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 2000079972	A5	20010510	AU 2000-79972	20001006
JP 2003527830	T2	20030924	JP 2001-528556	20001006

PRIORITY APPLN. INFO.: US 1999-158585P P 19991007
WO 2000-US27652 W 20001006

AB The present invention relates generally to nucleic acid and amino acid sequences of a fusion polypeptide comprising a Mycobacterium tuberculosis polypeptide, and a heterologous polypeptide of interest, expression vectors and host cells comprising such nucleic acids, and methods for producing such fusion polypeptides. In particular, the invention relates to materials and methods of using such M. tuberculosis sequence as a fusion partner to facilitate the stable and high yield expression of recombinant heterologous polypeptides of both eukaryotic and prokaryotic origin. A 14 kD C-terminal fragment (referred to as Ra12) of the Mycobacterium tuberculosis serine protease MTB32A can be expressed as a soluble protein. Use of the Ra12 sequences as a fusion partner is illustrated with construction of expression vectors, expression in Escherichia coli, and protein purification of a (His-tag) Ra12-DPPD fusion protein. Antiserum raised against the Ra12-DPPD fusion protein recognized the DPPD protein in immunoblotting anal. Ra12-WT1, Ra12-mammaglobin, and Ra12-H9-32A fusion proteins were also constructed and shorter or longer Ra12 sequences were fused with full length human mammaglobin gene sequences.

L22 ANSWER 20 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:228648 HCAPLUS
DOCUMENT NUMBER: 134:256837
TITLE: Therapeutic methods and compositions using viruses of the recombinant Paramyxoviridae family
INVENTOR(S): Russell, James; Cattaneo, Roberto; Peng, Kah-Whye; Schneider, Urs; Murphy, Anthea L.
PATENT ASSIGNEE(S): Mayo Foundation for Medical Education and Research, USA
SOURCE: PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001020989	A1	20010329	WO 2000-US26116	20000922
WO 2001020989	C2	20021003		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1217891 A1 20020703 EP 2000-965349 20000922
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL

PRIORITY APPLN. INFO.: US 1999-155873P P 19990922
WO 2000-US26116 W 20000922

AB The invention relates to compns. and methods for treating a patient having a tumor in order to reduce tumor size, comprising administering to the patient a replication-competent Paramyxoviridae virus comprising two or more of a) a nucleic acid sequence encoding a heterologous polypeptide, wherein upon administration the heterologous polypeptide is detectable in a biol. fluid of the patient, and detection of the heterologous polypeptide is indicative of Paramyxoviridae virus growth in the patient and reduction in tumor size; b) a recombinant F protein, H protein, or M protein of Paramyxoviridae virus that increases fusogenicity of virus with cells; c) a nucleic acid sequence encoding a cytokine; and d) a Paramyxoviridae virus that is specific for cells of the tumor.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 21 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:168113 HCAPLUS
DOCUMENT NUMBER: 134:217996
TITLE: Expression vector systems for expression and activation of serine protease zymogens
INVENTOR(S): Darrow, Andrew; Qi, Jenson; Andrade-Gordon, Patricia
PATENT ASSIGNEE(S): Ortho-McNeil Pharmaceutical, Inc., USA
SOURCE: PCT Int. Appl., 174 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001016289	A2	20010308	WO 2000-US22283	20000814
WO 2001016289	A3	20010907		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6420157 B1 20020716 US 1999-386642 19990831
EP 1214400 A2 20020619 EP 2000-955526 20000814
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL

JP 2003508045 T2 20030304 JP 2001-520837 20000814
PRIORITY APPLN. INFO.: US 1999-386642 A 19990831
US 1999-303162 A2 19990430
WO 2000-US22283 W 20000814

AB DNA sequences are provided encoding an expression vector system that will permit, through limited proteolysis, the activation of expressed zymogen precursor of (S1) serine proteases in a highly controlled and reproducible fashion. Nucleic acids encoding pre sequences derived of prolactin and trypsinogen, and pro sequences derived from the EK **cleavage site** of human trypsinogen I or blood-coagulation factor Xa, are provided. The processed expressed protein, once activated, is rendered in a form amenable to measuring the catalytic activity. This catalytic activity of the activated form, is often a more accurate representation of the mature S1 protease gene product relative to the unprocessed zymogen precursor. Thus, this series of zymogen activation constructs represents a significant system for the anal. and characterization of serine protease gene products. Proteases prostasin, O, neuropsin, F, and MH2 are prepared which may be used in pharmaceutical compns., for the identification of physiol. substrates and specific modulators, for laundry detergents, and in skin care products.

L22 ANSWER 22 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:152855 HCAPLUS
DOCUMENT NUMBER: 134:203683
TITLE: Recombinant construction and expression of single-chain activatable neurotoxins
INVENTOR(S): Dolly, J. Oliver; Li, Yan; Chan, Kuo Chion
PATENT ASSIGNEE(S): Allergan Sales, Inc., USA
SOURCE: PCT Int. Appl., 90 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001014570	A1	20010301	WO 2000-US23427	20000825
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000012759	A	20020402	BR 2000-12759	20000825
EP 1206554	A1	20020522	EP 2000-964920	20000825
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003507073	T2	20030225	JP 2001-518882	20000825

PRIORITY APPLN. INFO.: US 1999-150710P P 19990825
WO 2000-US23427 W 20000825

AB Compns. comprising activable recombinant neurotoxins and polypeptides derived therefrom. The invention also comprises nucleic acids encoding such polypeptides, and methods of making such polypeptides and nucleic acids. Thus, a single-chain protein is constructed by genetic engineering techniques comprising the functional domains of a clostridial neurotoxin H

chain and some or all of the functions of a clostridial neurotoxin L chain, and having an inserted proteolytic **cleavage site** located between the H domain and the L domain by which the single-chain protein may be cleaved to produce the individual chains, prefereably covalently linked by a disulfide linkage. To minimize the safety risk associated with handling neurotoxins, they are expressed as their low activity (or inactive) single-chian proforms, and then carefully activated via **cleavage** at a **site** designed to have a high degree of specificity to proteolytic enzymes which do not normally occur in humans. The interchain loop region of the Clostridium botulinum subtype E neurotoxin, which is normally resistant to proteolytic nicking in the bacterium and mammals, is modified to include the inserted proteolytic **cleavage site**. Single-chain tetanus toxins containing a bovine **enterokinase cleavage site** are expressed from Escherichia coli and shown to induce in vitro paralysis using the mouse phrenic nerve hemi-diaphragm assay. Further modification of single-chain tetanus toxin to remove proteolytic **cleavage sites** reduces the toxicity of unnicked recombinant toxin. Single-chain botulin type A and E neurotoxins are also described.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 23 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:861808 HCAPLUS
DOCUMENT NUMBER: 134:37936
TITLE: Protein and cDNA sequences encoding human and mouse four-helical bundle cytokine zsig81, and uses thereof
INVENTOR(S): Piddington, Christopher S.; West, James R.; Holly, Richard D.; Burkhead, Steven K.
PATENT ASSIGNEE(S): Zymogenetics, Inc., USA
SOURCE: PCT Int. Appl., 109 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000073459	A1	20001207	WO 2000-US15002	20000601
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1181369	A1	20020227	EP 2000-942653	20000601
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2003501034	T2	20030114	JP 2001-500771	20000601

PRIORITY APPLN. INFO.: US 1999-323582 A 19990601
WO 2000-US15002 W 20000601

AB This present invention provides protein and cDNA sequences encoding human and mouse four-helical bundle cytokine. The cytokine has been designated zsig81, and has restricted expression in primarily heart, lung and liver and its encoding gene has been mapped to human chromosome 7 (7q32-33) .

Zsig81 has been shown to stimulate proliferation of hematopoietic cells and will be useful expansion of these cells, as well as conditions associated with hematopoietic cells. The invention is directed to antibodies and methods of making zsig81 polypeptides, as well.

L22 ANSWER 24 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:646155 HCAPLUS
DOCUMENT NUMBER: 133:248048
TITLE: Manufacture of proteins as **fusion** proteins with the self-association domain of human glucagon
INVENTOR(S): Park, Young Hoon; Lee, Jeewon; Kim, Dae-Young
PATENT ASSIGNEE(S): Korea Research Institute of Bioscience and Biotechnology, S. Korea; Hanwha Chemical Corporation
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000053777	A1	20000914	WO 2000-KR187	20000309
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
KR 2000059787	A	20001005	KR 1999-7641	19990309

PRIORITY APPLN. INFO.: KR 1999-7641 A 19990309
AB A method of manufacturing proteins as complexes by synthesizing them as **fusion** proteins with the self-association peptide of human glucagon is described. The glucagon moiety is at the N-terminal end of the **fusion** protein and is linked to the target protein by a **linker** including a **proteinase cleavage site**. Use of glucagon to manufacture human interleukin 2 as inclusion bodies in Escherichia coli is demonstrated. Use of the self-association domain of glucagon lowered the degree of non-specific binding of other proteins by the interleukin.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 25 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:592843 HCAPLUS
DOCUMENT NUMBER: 133:182929
TITLE: Fusion proteins of the collagen-binding fragment of human fibronectin ligated to physiologically active polypeptides
INVENTOR(S): Ishikawa, Tetsuya; Kitajima, Takashi
PATENT ASSIGNEE(S): Terumo Kabushiki Kaisha, Japan
SOURCE: PCT Int. Appl., 135 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2

Search completed by David Schreiber 308-4292

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000049159	A1	20000824	WO 2000-JP964	20000221
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
JP 2001190280	A2	20010717	JP 2000-41142	20000218
AU 2000025750	A5	20000904	AU 2000-25750	20000221
EP 1151116	A1	20011107	EP 2000-904061	20000221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: JP 1999-41913 A 19990219
JP 1999-311364 A 19991101
WO 2000-JP964 W 20000221

AB A collagen-binding physiol. active polypeptide is provided. In this polypeptide, a peptide from fibronectin is ligated to a physiol. active peptide, and this hybrid polypeptide is provided with both the collagen-binding activity and the physiol. activity. A novel collagen matrix wherein the hybrid polypeptide is combined with collagen is also provided. The collagen-binding physiol. active polypeptide provided with both the collagen-binding activity and the physiol. activity is useful as a drug delivery system (DDS) of the physiol. active peptide. Furthermore, this polypeptide can be combined with collagen to provide a functionally modified collagen matrix which is quite useful as a new biomaterial adapted for use in tissue regeneration. Thus, chimeric proteins are constructed with an initiator methionine residue linked to the collagen-binding domain (residues 260-599) of human fibronectin, further linked to ligation residues Leu and Asp, followed by an **enterokinase** recognition/**cleavage site** (Asp-Asp-Asp-Asp-Lys), followed by the amino acid sequence for either human basic fibroblast growth factor or epidermal growth factor.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 26 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:368620 HCAPLUS
DOCUMENT NUMBER: 133:13412
TITLE: Protein expression vector with secretory signal sequence, Tag sequence, and cleavable sequence, and
INVENTOR(S): **Uemura, Hidetoshi; Okui, Akira; Kominami, Katsuya; Yamaguchi, Nozomi ; Mitsui, Shinichi**
PATENT ASSIGNEE(S): Fuso Pharmaceutical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2000031284	A1	20000602	WO 1999-JP6474	19991119	
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1132479	A1	20010912	EP 1999-972690	19991119	
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: JP 1998-331515 A 19981120
WO 1999-JP6474 W 19991119

AB A protein expression vector characterized by containing a secretory signal sequence and, in the 3'-downstream side thereof, a Tag sequence, a scissile or cleavable sequence and a cloning site, into which a nucleic acid sequence encoding a target protein can be inserted, in this order, is disclosed. The vector may contain a spacer sequence 3' of the secretory signal sequence, which could be a scissile nucleic acid sequence. The scissile nucleic acid sequence is cleavable with **enterokinase**, and the secretory signal sequence may be IgG(κ) signal or a trypsin signal sequence. The Tag nucleic acid sequence is preferably a polyhistidine and may addnl. contain an epitope coding sequence. The target protein may be human active **neurosin**. Methods and compns. for producing a recombinant target protein, possibly as a fusion protein are also claimed. These expression vectors directs secretion of recombinant proteins into the culture medium of infected insect cells. By providing a vector-encoded signal peptide upstream from a multiple cloning site, the product of the inserted cDNA is directed to the secretory pathway. In addition, a C-terminal His-tag allows convenient purification of the native protein directly from the culture medium in less than 5 h. The His-tag can be cleaved off the purified protein by utilizing an **enterokinase cleavage site** located directly C-terminal to the His sequence. By insertion of a coding sequence representing the human active **neurosin** into the expression vectors, a high level of protein synthesis was demonstrated in COS-1 and Sf9 cells with either IgG(κ) signal or a trypsin signal sequence. The high level of production and the ease with which native protein can be purified almost to homogeneity, makes these expression vectors particularly suitable for protein synthesis and purification

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 27 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:718875 HCAPLUS
DOCUMENT NUMBER: 131:348774
TITLE: Tandem fluorescent protein constructs and their preparation for enzyme assays
INVENTOR(S): Tsien, Roger Y.; Heim, Roger; Cubitt, Andrew
PATENT ASSIGNEE(S): The Regents of the University of California, USA; Aurora Biosciences Corporation
SOURCE: U.S., 33 pp., Cont.-in-part of U.S. Ser. No. 594,575. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English

Search completed by David Schreiber 308-4292

FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5981200	A	19991109	US 1997-792553	19970131
ES 2177939	T3	20021216	ES 1997-905667	19970131
US 2003186229	A1	20031002	US 2001-865291	20010524
US 2002164674	A1	20021107	US 2002-57505	20020125

PRIORITY APPLN. INFO.: US 1996-594575 A2 19960131
US 1997-792553 A1 19970131
US 1999-396003 B2 19990913

AB This invention provides tandem fluorescent protein construct including a donor fluorescent protein moiety, an acceptor fluorescent protein moiety and a linker moiety that couples the donor and acceptor moieties. The donor and acceptor moieties exhibit fluorescence resonance energy transfer which is eliminated upon cleavage. The constructs are useful in enzymic assays. Mutant green fluorescent proteins (GFPs) were created by mutagenesis of the Aequorea victoria GFP. Polyhistidine tagged tandem green and blue fluorescent proteins were recombinantly constructed having an inserted peptide sequence including **cleavage** recognition **sites** for many proteases. Cleavage expts. were done with trypsin, **enterokinase** and calpain.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 28 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:688099 HCAPLUS
DOCUMENT NUMBER: 132:45555
TITLE: Toxins that are activated by HIV type-1 protease through removal of a signal for degradation by the N-end-rule pathway
AUTHOR(S): Falnes, Pal O.; Welker, Reinhold; Krausslich, Hans-Georg; Olsnes, Sjur
CORPORATE SOURCE: Institute for Cancer Research, The Norwegian Radium Hospital, Oslo, 0310, Norway
SOURCE: Biochemical Journal (1999), 343(1), 199-207
CODEN: BIJOAK; ISSN: 0264-6021
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Diphtheria toxin enters the cytosol of mammalian cells where it inhibits cellular protein synthesis, leading to cell death. Recently we found that the addition of a signal for N-end-rule-mediated protein degradation to diphtheria toxin substantially reduced its intracellular stability and toxicity. These results prompted us to construct a toxin containing a degradation signal that is removable through the action of a viral protease. In principle, such a toxin would be preferentially stabilized, and thus activated, in cells expressing the viral protease in the cytosol, i.e. virus-infected cells, thereby providing a specific eradication of these cells. In the present work we describe the construction of toxins that contain a signal for N-end-rule-mediated degradation just upstream of a **cleavage site** for the **protease** from HIV type 1 (HIV-1 PR). We show that the toxins are cleaved by HIV-1 PR exclusively at the introduced sites, and thereby are converted from unstable to stable proteins. Furthermore, this cleavage substantially increased the ability of the toxins to inhibit cellular protein synthesis. However, the toxins were unable to selectively eradicate HIV-1-infected cells, apparently due

to low cytosolic HIV-1 PR activity, since we could not detect cleavage of the toxins by HIV-1 PR in infected cells. Alternative strategies for the construction of toxins that can specifically be activated by viral proteases are discussed.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 29 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:45068 HCAPLUS
DOCUMENT NUMBER: 130:115003
TITLE: Recombinant cloning and fermentative production of a rabbit tissue factor fusion protein
INVENTOR(S): Novy, Robert E., Jr.; Domanico, Michael J.; Yaeger, Keith W.; Kroeker, Warren
PATENT ASSIGNEE(S): Pel-Freez, USA
SOURCE: U.S., 13 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5858724	A	19990112	US 1996-683007	19960716

PRIORITY APPLN. INFO.: US 1996-683007 19960716

AB Recombinant rabbit tissue factor (RTF) is cloned and produced in a bacterial host. This protein, which is relatively insol. and has several disulfide bonds, requires special modifications in order to express and be purified at com. levels. By expressing the tissue factor as a fusion protein with a bacterial enzyme, thioredoxin, solubility is increased. Thus, a chimeric gene is constructed in which nucleotides 1-327 encode E. coli thioredoxin A, nucleotides 349-366 encode the His.Tag marker, nucleotides 376-393 encode a thrombin **cleavage site**, nucleotides 400-444 encode the RNase A S-peptide marker protein, nucleotides 460-474 encode an **enterokinase cleavage site**, and nucleotides 505-1224 encode a truncated RTF open reading frame. Use of a thioredoxin reductase-deficient host aids in proper tertiary structure for biol. activity.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 30 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:712369 HCAPLUS
DOCUMENT NUMBER: 129:327215
TITLE: Preparation of highly purified mocarhagin and cloning of a cDNA encoding it and therapeutics uses of the enzyme
INVENTOR(S): Boodhoo, Amechand; Seehra, Jasbir S.; Shaw, Gray; Sako, Dianne
PATENT ASSIGNEE(S): Genetics Institute, Inc., USA
SOURCE: PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9846771	A2	19981022	WO 1998-US7998	19980414
WO 9846771	A3	19990211		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9872525	A1	19981111	AU 1998-72525	19980414

PRIORITY APPLN. INFO.:	US 1997-843373 A	19970415
	US 1998-12637 A	19980123
	US 1998-26001 A	19980218
	WO 1998-US7998 W	19980414

AB Methods of purifying the cobra venom proteinase mocarhagin to near-homogeneity and cloning of a cDNA encoding it are described. The enzyme hydrolyzes a number of proteins involved in cell adhesion and platelet agglutination and may be useful in the treatment of disorders such as restenosis. Crude venom was fractionated by affinity chromatog. against immobilized heparin; by size exclusion chromatog.; and by ion-exchange chromatog. against a Mono-S column. Yield of mocarhagin was 2-3 mg/gm venom and purity was >95%. A cDNA was cloned from a N. mossambica mossambica venom gland library by PCR using amino acid sequence-derived probes. The protein was manufactured by expression of a cDNA encoding an analog containing a **cleavage site** for **enterokinase** at the C-terminus of the signal peptide in COS cells. **Enterokinase** cleavage of the precursor to the mature form was demonstrated.

L22 ANSWER 31 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER:	1998:448999 HCAPLUS
DOCUMENT NUMBER:	129:174702
TITLE:	High-level production of human growth hormone in Escherichia coli by a simple recombinant process
AUTHOR(S):	Shin, Nam-Kyu; Kim, Dae-Young; Shin, Chul-Soo; Hong, Min-Sun; Lee, Jeewon; Shin, Hang-Cheol
CORPORATE SOURCE:	Laboratories of Protein Engineering and Bioprocess Engineering, Hanhyo Institute of Technology, Taejon, 305-390, S. Korea
SOURCE:	Journal of Biotechnology (1998), 62(2), 143-151 CODEN: JBITD4; ISSN: 0168-1656
PUBLISHER:	Elsevier Science B.V.
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB Procedures have been devised for producing in Escherichia coli high yields of purified recombinant human growth hormone (hGH), by utilizing N-terminal pentapeptide sequence of human tumor necrosis factor-alpha, histidine tag and **enterokinase cleavage site** as a fusion partner. The fusion protein was produced as a soluble protein at the beginning of gene expression, but progressively became insol. in Escherichia coli cytoplasm. The insol. protein was solubilized by simple alkaline pH shift and purified to near homogeneity by Ni2+-chelated affinity chromatog. Following specific **enterokinase** cleavage, the recombinant hGH was purified by one-step anion exchange chromatog. The ease and speed of this recombinant process, as well as the high productivity, makes it adaptable to the large-scale production of hGH. Moreover, the highly efficient fusion partner could be applied to the

production of other therapeutically important proteins.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 32 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:106044 HCAPLUS
DOCUMENT NUMBER: 128:176945
TITLE: Manufacture of biologically active peptides as precursors in Bordetella with subsequent processing with a proteinase manufactured in a second host
INVENTOR(S): Maslikova, Alla Nikolaevna; Nechaev, Viktor Nikolaevich; Fedchenko, Valery Ivanovich; Guriev, Sergei Olegovich; Sivov, Igor Gennadievich
PATENT ASSIGNEE(S): Firma "Nika-Universal", Russia; Maslikova, Alla Nikolaevna; Nechaev, Viktor Nikolaevich; Fedchenko, Valery Ivanovich; Guriev, Sergei Olegovich; Sivov, Igor Gennadievich
SOURCE: PCT Int. Appl., 306 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Russian
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9804731	A1	19980205	WO 1996-RU198	19960725
W: AU, CA, CN, EE, GE, JP, KG, KP, KR, LT, LV, MD, MN, MX, NO, NZ, PL, RU, US, UZ, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9711125	A1	19980220	AU 1997-11125	19960725

PRIORITY APPLN. INFO.: WO 1996-RU198 19960725

AB A method of manufacturing biol. active peptides in a Bordetella expression host is described. The peptides are manufactured as a precursor that is subsequently processed with a proteinase manufactured in a sep. host, e.g. Proteus, to release the biol. active peptide. The host for manufacture of this protein may have the Lon proteinase inactivated to prevent degradation of the **fusion** protein in the host. The protein is subsequently processed in vitro using a **proteinase** that recognizes **cleavage sites** built into the **fusion** protein. The method can be used to manufacture peptides that may be toxic to the host by controlling the expression of the gene for the processing proteinase. The preferred carrier for the peptide, i.e. the **fusion** partner, is a camphor-oxidizing cytochrome P 450 of Bordetella. Methods of integrating plasmids containing two replicons into the Bordetella chromosome by recombination at repeated sequences on the host chromosome are also described. This invention further relates to an expression vector using the phasmid pT72. The present invention finally relates to a method for producing circular genomes of bacteriophage T7 and the development of overproducer expression hosts. Manufacture of human proinsulin as a **fusion** protein with Pseudomonas cytochrome P 450 and its subsequent processing are demonstrated.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 33 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:75999 HCAPLUS
DOCUMENT NUMBER: 128:150383
TITLE: Adenoviral-mediated cell targeting commanded by the

adenovirus penton base protein
INVENTOR(S): Wickham, Thomas J.; Kovesdi, Imre; Roelvink, Petrus W.; Brough, Douglas E.; McVey, Duncan L.; Bruder, Joseph T.
PATENT ASSIGNEE(S): Genvec, Inc., USA
SOURCE: U.S., 56 pp., Cont.-in-part of U.S. 5,559,099.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5712136	A	19980127	US 1996-634060	19960417
US 5559099	A	19960924	US 1994-303162	19940908
CA 2198861	AA	19960314	CA 1995-2198861	19950807
US 5962311	A	19991005	US 1996-700846	19960821
US 5731190	A	19980324	US 1996-709515	19960906
US 6465253	B1	20021015	US 1999-101751	19990129
US 2003022355	A1	20030130	US 2001-999724	20011024

PRIORITY APPLN. INFO.:
US 1994-303162 A2 19940908
US 1995-563368 A2 19951128
US 1996-634060 A2 19960417
US 1996-700124 A2 19960821
US 1996-700846 A2 19960821
US 1996-701124 A2 19960821
WO 1996-US19150 W 19961127
US 1999-101751 A1 19990129

AB A method of introducing an adenovirus into a cell comprises a particular cell surface binding site as well as a chimeric adenovirus penton base protein, and recombinant adenoviral vectors comprising the chimeric adenovirus penton base protein for use in the method are provided. The adenovirus is contacted with a bispecific mol. (antibody) comprising (1) a component that selectively binds to a domain of the penton base protein of the adenovirus, and (2) a second component that selectively binds the particular cell surface site. Binding of the fiber protein of the adenovirus to any cell surface mol. is abrogated (e.g., by the introduction of a **protease cleavage site**), and the cell binds to a specific site introduced into the penton base protein of the adenovirus. The construction of chimeric adenovirus penton base protein and recombinant adenoviral vectors is described.

REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 34 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:650373 HCAPLUS
DOCUMENT NUMBER: 127:328387
TITLE: Precursors of catalytic antibodies
INVENTOR(S): Koentgen, Frank; Suess, Gabriele Maria; Tarlinton, David Mathew; Treutlein, Herbert Rudolf
PATENT ASSIGNEE(S): Amrad Operations Pty. Ltd., Australia; Koentgen, Frank; Suess, Gabriele Maria; Tarlinton, David Mathew; Treutlein, Herbert Rudolf
SOURCE: PCT Int. Appl., 109 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9735887	A1	19971002	WO 1997-AU194	19970326
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2249455	AA	19971002	CA 1997-2249455	19970326
AU 9721434	A1	19971017	AU 1997-21434	19970326
AU 731580	B2	20010405		
ZA 9702620	A	19971120	ZA 1997-2620	19970326
GB 2326643	A1	19981230	GB 1998-20966	19970326
GB 2326643	B2	20000927		
EP 935612	A1	19990818	EP 1997-913981	19970326
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6043069	A	20000328	US 1997-828741	19970326
JP 2000507105	T2	20000613	JP 1997-533873	19970326
US 6326179	B1	20011204	US 1998-160567	19980925
US 6521741	B1	20030218	US 2000-710299	20001109

PRIORITY APPLN. INFO.:

AU 1996-8951	A	19960326
AU 1997-5375	A	19970227
US 1997-828741	A1	19970326
WO 1997-AU194	W	19970326
US 1998-160567	A3	19980925

AB The invention is directed to growth factors or precursors of catalytic antibodies comprising a B-cell surface mol. binding portion, which can induce B-cell mitogenesis. The preferred B-cell surface mol. binding portions are the Ig binding mols. of protein L from Peptostreptococcus magnus, protein A, protein G and protein H. The growth factor having an ability to induce B-cell mitogenesis can be further linked to a target antigen to which catalytic antibodies are sought. B-cell mitogenesis is then dependent on the catalytic cleavage of the antigen portion of the growth factor by catalytic antibodies on the surface of B cells. The method of the present invention is useful for generating catalytic antibodies for both therapeutic and diagnostic purposes. Vector pASK75 expressing growth factor protein LHL containing P. magnus protein L and hen egg lysozyme was prepared and expressed in Escherichia coli, and LHL was purified. A form of LHL protein carrying the N-terminal FLAG epitope and the C-terminal strep-tag was generated and tested for B cell mitogenic activity. Similarly, the growth factor precursor CATAB comprises a tumor necrosis factor flanked LHL with the variable region from an Ig κ or λ light chain further masking the B surface Ig binding domain of the L mols. TLHL comprises a variable κ light chain linked to the N-terminus of an amino acid **linker** sequence comprising the tobacco etch virus **protease cleavage site** which is in turn linked to LHL.

L22 ANSWER 35 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:599329 HCAPLUS
DOCUMENT NUMBER: 125:239644
TITLE: Production of recombinant human glucagon in Escherichia coli by a novel fusion protein approach

AUTHOR(S): Kim, Dae-Young; Shin, Nam-Kyu; Chang, Seung-Gu; Shin, Hang-Cheol
CORPORATE SOURCE: Protein Eng. Lab., Hanhyo Inst. Technol., Kyungki-Do, S. Korea
SOURCE: Biotechnology Techniques (1996), 10(9), 669-672
CODEN: BTECE6; ISSN: 0951-208X
PUBLISHER: Chapman and Hall
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A novel approach to the production of a human glucagon in E. coli is described. The 29 amino acids of human glucagon and pentapeptide linker containing enzyme processing site were fused at the amino terminus to a 57 residue N-terminal portion of the human tumor necrosis factor-alpha (hTNF-α). The fusion protein was expressed in the E. coli cytoplasm at levels up to 30% of the total cell protein. Precipitation of the fusion protein near its isoelec. point, specific **enterokinase cleavage** at the linker **site** and subsequent HPLC purification makes this approach suitable for the production of glucagon as well as other relatively small peptides with therapeutic interests.

L22 ANSWER 36 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:998287 HCAPLUS
DOCUMENT NUMBER: 124:76529
TITLE: Heparin-binding protein and its preparation for the treatment of sepsis
INVENTOR(S): Flodgaard, Hans Jakob Hem; Rasmussen, Poul Baad
PATENT ASSIGNEE(S): Novo Nordisk A/S, Den.
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9528949	A1	19951102	WO 1995-DK121	19950317
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TT, UA				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2188395	AA	19951102	CA 1995-2188395	19950317
AU 9523033	A1	19951116	AU 1995-23033	19950317
AU 703963	B2	19990401		
EP 762889	A1	19970319	EP 1995-916583	19950317
EP 762889	B1	20030507		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
CN 1146724	A	19970402	CN 1995-192688	19950317
HU 75557	A2	19970528	HU 1996-2895	19950317
JP 09512168	T2	19971209	JP 1995-527282	19950317
NZ 332683	A	20010629	NZ 1995-332683	19950317
CZ 289439	B6	20020116	CZ 1996-3082	19950317
RU 2200573	C2	20030320	RU 1996-122777	19950317
AT 239494	E	20030515	AT 1995-916583	19950317
FI 9604227	A	19961021	FI 1996-4227	19961021
NO 9604465	A	19961021	NO 1996-4465	19961021

PRIORITY APPLN. INFO.:

DK 1994-464	A	19940421
DK 1994-1452	A	19941221
WO 1995-DK121	W	19950317

AB A pharmaceutical composition is claimed for the prevention or treatment of diseases or conditions associated with induction of the cytokine cascade by lipopolysaccharide (LPS), the composition comprising a heparin-binding protein (HBP) which, in glycosylated form, has an apparent mol. weight of 28 kD (as determined by SDS-PAGE under reducing conditions), the protein being produced in the azurophil granules of polymorphonuclear leukocytes, together with a pharmaceutically acceptable carrier or diluent. The heparin-binding protein is produced in host cells containing a DNA sequence encoding N-terminally extended HBP or encoding HBP preceded by and fused to a DNA sequence encoding another protein. Also disclosed is a process wherein the culture medium contains a sulfated polysaccharide such as heparin.

L22 ANSWER 37 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:951242 HCAPLUS
DOCUMENT NUMBER: 124:84915
TITLE: **Fusion** products of interleukin 3 with hematopoietic growth factors and their manufacture for therapeutic use
INVENTOR(S): Bauer, Christopher S.; Abrams, Mark Allen; Braford-Goldberg, Sarah Ruth; Caparon, Marie Helena; Easton, Alan Michael; Klein, Barbara Kure; Mc, Kearn John Patrick; Olins, Peter O.; Paik, Kumnan; Thomas, John Warren
PATENT ASSIGNEE(S): G. D. Searle and Co., USA
SOURCE: PCT Int. Appl., 447 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 17
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9521254	A1	19950810	WO 1995-US1185	19950202
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6057133	A	20000502	US 1994 192325	19940204
AU 9518356	A1	19950821	AU 1995-18356	19950202
AU 697433	B2	19981008		
EP 742826	A1	19961120	EP 1995-910141	19950202
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
BR 9506733	A	19970923	BR 1995-6733	19950202
JP 10502801	T2	19980317	JP 1995-520671	19950202
RO 118016	B1	20021230	RO 1996-1594	19950202
US 6022535	A	20000208	US 1995-469318	19950606
US 6030812	A	20000229	US 1995-468609	19950606
US 6361977	B1	20020326	US 1995-446872	19950606
NO 9603225	A	19960925	NO 1996-3225	19960801
FI 9603072	A	19960802	FI 1996-3072	19960802
US 6436387	B1	20020820	US 1996-762227	19961209
US 2003185790	A1	20031002	US 2002-83446	20020226

Search completed by David Schreiber 308-4292

PRIORITY APPLN. INFO.:

US 1994-192325	A2	19940204
US 1992-981044	B2	19921124
WO 1993-US11197	A2	19931122
WO 1995-US1185	W	19950202
US 1995-411795	A2	19950406
US 1995-446872	A2	19950606
US 1996-762227	A3	19961209

AB Human interleukin-3 (hIL-3) variants fused with other colony stimulating factors (CSF), cytokines, lymphokines, interleukins, hematopoietic growth factors or IL-3 variants are described. These variants and **fusion** proteins are intended for use in the stimulation of hematopoiesis in support of chemotherapy of cancer, notably of leukemias and B-lymphomas. The IL-3 variants may have 1-14 N- or 1-15 C-terminal deletions and have 4-26 addnl. amino acid substitutions. A **linker** peptide derived from an Ig hinge region can be used to join the domains of the **fusion** protein and a **proteinase cleavage site** may be incorporated into the **linker** region. The construction of expression vectors for manufacture of these **fusion** proteins in Escherichia coli is described. A number of **fusion** proteins were tested and found to show the biol. activities expected of both moieties.

L22 ANSWER 38 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1995:109775 HCAPLUS
DOCUMENT NUMBER: 122:24828
TITLE: High-efficiency synthesis of human α-endorphin and magainin in the erythrocytes of transgenic mice: a production system for therapeutic peptides
AUTHOR(S): Sharma, Ajay; Khoury-Christianson, M. Khoury; White, Steven P.; Dhanjal, Nirpal K.; Huang, Wen; Paulhiac, Clara; Friedman, Eric J.; Manjula, Belur N.; Kumar, Ramesh
CORPORATE SOURCE: DNX Biotherapeutics Inc., Princeton, NJ, 08540, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1994), 91(20), 9337-41
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Chem. synthesis of peptides, though feasible, is hindered by consideration of cost, purity, and efficiency of synthesizing longer chains. Here the authors describe a transgenic system for producing peptides of therapeutic interest as fusion proteins at low cost and high purity. Transgenic Hb expression technol. using the locus control region was employed to produce fusion Hbs in the erythrocytes of mice. The fusion Hb contains the desired peptide as an extension at the C end of human α-globin. A protein **cleavage site** is inserted between the C end of the α-globin chain and the N-terminal residue of the desired peptide. The peptide is recovered after cleavage of the fusion protein with enzymes that recognized this cleavage signal as their substrate. Due to the selective compartmentalization of Hb in the erythrocytes, purification of the fusion Hb is easy and efficient. Because of its compact and highly-ordered structure, the internal sites of Hb are resistant to protease digestion and the desired peptide is efficiently released and recovered. The applicability of this approach was established by producing a 16-mer α-endorphin peptide and a 26-mer magainin peptide in transgenic mice. Transgenic animals and their progeny expressing these fusion proteins remain healthy, even when the fusion protein is expressed at >25% of the total Hb in the erythrocytes. Addnl. applications and potential improvements of this methodol. are discussed.

L22 ANSWER 39 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1994:450086 HCAPLUS
DOCUMENT NUMBER: 121:50086
TITLE: Method of treating cell damage or depletion
INVENTOR(S): Williams, David A.; Clark, Steven C.
PATENT ASSIGNEE(S): Genetics Institute, Inc., USA
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9405318	A1	19940317	WO 1993-US8247	19930901
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5460810	A	19951024	US 1992-941372	19920902
EP 671934	A1	19950920	EP 1993-920456	19930901
EP 671934	B1	20001220		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08500838	T2	19960130	JP 1993-507428	19930901
JP 2828778	B2	19981125		
AU 677236	B2	19970417	AU 1993-50999	19930901
AU 9350999	A1	19940329		
AT 198158	E	20010115	AT 1993-920456	19930901
ES 2155834	T3	20010601	ES 1993-920456	19930901

PRIORITY APPLN. INFO.: US 1992-941372 A 19920902
WO 1993-US8247 W 19930901

AB A method of restoring damaged or depleted cell populations by treating the patient with cytokines, particularly IL-11 and IL-6 is described. The treatment is particularly intended for amelioration of the effects of chemotherapeutics on rapidly dividing tissues. Human interleukin 11 was manufactured as a fusion protein with Escherichia coli thioredoxin; the protein was linked by an **enterokinase cleavage site** that allowed specific **cleavage** of the fusion protein and recovery of interleukin 11. Mice treated with 6.0 Gy therapeutic X-rays were treated with human IL-11 at 250 μg/kg/day. Mice treated with IL-11 showed fewer hepatic bacterial foci than controls although diarrhea was no less marked. IL-11 treated mice showed better survival although there were no differences in peripheral white blood cell or platelet counts between test and control animals. IL-11 treated animals showed nearly normal crypt depth and villus length and an improved recovery of mitotic activity in crypts.

L22 ANSWER 40 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1994:402609 HCAPLUS
DOCUMENT NUMBER: 121:2609
TITLE: Manufacture of proteins as fusions with thioredoxin and thioredoxin-like proteins
INVENTOR(S): Mccoy, John; Lavallie, Edward R.
PATENT ASSIGNEE(S): Genetics Institute, Inc., USA
SOURCE: U.S., 38 pp. Cont.-in-part of U.S. Ser. No. 745,382.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5292646	A	19940308	US 1992-921848	19920728
US 5270181	A	19931214	US 1991-745382	19910814
CA 2093643	AA	19920807	CA 1992-2093643	19920206
CA 2093643	C	20011030		
EP 1231275	A2	20020814	EP 2002-6659	19920206
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC				
EP 1231217	A2	20020814	EP 2002-6660	19920206
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC				
WO 9402502	A1	19940203	WO 1993-US6913	19930723
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9347814	A1	19940214	AU 1993-47814	19930723
US 5646016	A	19970708	US 1993-165301	19931210
US 6143524	A	20001107	US 1997-810436	19970304

PRIORITY APPLN. INFO.:

US 1991-652531	B2	19910206
US 1991-745382	A2	19910814
EP 1992-907803	A3	19920206
US 1992-921848	A	19920728
WO 1993-US6913	W	19930723
US 1993-165301	A3	19931210

AB Proteins are manufactured as fusions with a thioredoxin-like protein by expression of the chimeric gene in a microbial host. The protein may be fused to the N- or C- terminus of the thioredoxin-like mol., or within the thioredoxin-like mol., for example at the active-site loop. The gene is expressed from a strong promoter. The fusion protein accumulates in the bacterial cytoplasm and may be selectively released from the cell by osmotic shock or freeze/thaw procedures and may be cleaved to liberate the soluble, correctly folded heterologous protein from the thioredoxin-like portion. A chimeric gene for a fusion protein of Escherichia coli thioredoxin and human interleukin-11 connected via a spacer containing a **cleavage site** for **enterokinase** under control of the pL promoter was constructed and expressed in E. coli. The protein accumulated in the cytoplasm without forming inclusion bodies and was purified from lysates chromatog. The fusion protein had an interferon activity of 8+105 units/mg; after cleavage with **enterokinase** , the activity of the IL-11 fragment was 2.5+106 units/mg, which is similar to that of IL-11 from COS cells.

L22 ANSWER 41 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1992:209124 HCAPLUS
DOCUMENT NUMBER: 116:209124
TITLE: Affinity peptides for use in the purification of **fusion** proteins from transgenic hosts
INVENTOR(S): Coolidge, Thomas R.; Wagner, Fred; Van Heeke, Gino; Schuster, Sheldon M.; Stout, Jay; Wylie, Dwane E.
PATENT ASSIGNEE(S): Bionebraska, Inc., USA
SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9201707	A1	19920206	WO 1991-US4511	19910624
W: AU, CA, FI, JP, NO				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
US 5595887	A	19970121	US 1990-552810	19900716
AU 9189155	A1	19920218	AU 1991-89155	19910624
AU 662302	B2	19950831		
EP 539530	A1	19930505	EP 1992-902529	19910624
EP 539530	B1	20000202		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT 189478	E	20000215	AT 1992-902529	19910624
JP 3129437	B2	20010129	JP 1992-500610	19910624
CA 2087261	C	20021224	CA 1991-2087261	19910624
PRIORITY APPLN. INFO.:			US 1990-552810 A	19900716
			WO 1991-US4511 W	19910624

AB A method is described for the preparation of heterologous proteins in transgenic hosts as a **fusion** product with a short peptide that includes a ligand-binding domain and a flexible peptide that acts as a bridge and includes a **protease cleavage site** . Chimeric genes encoding **fusion** proteins of human carbonic anhydrase as affinity ligand and short peptides including angiotensin, a calcitonin derivative, bovine caltrin, and small subunits of the Escherichia coli ATPase with the bridging peptide including an **enterokinase cleavage site** were prepared These genes were expressed from a T7 promoter, and the protein was recovered by affinity chromatog. on immobilized sulfanilamide and cleaved with **enterokinase**.

L22 ANSWER 42 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER:	1992:52965 HCAPLUS
DOCUMENT NUMBER:	116:52965
TITLE:	Method for manufacture of recombinant insulin-like growth factor 1
INVENTOR(S):	Lee, Young Ik; Kwak, Ju Won; Park, Heui Dong; Young, Im Suhn; Hoon, Kim Young; Sun, Yoon Mi
PATENT ASSIGNEE(S):	Korea Institute of Science and Technology, S. Korea
SOURCE:	Brit. UK Pat. Appl., 36 pp. CODEN: BAXXDU
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2241703	A1	19910911	GB 1991-4524	19910304
JP 06113878	A2	19940426	JP 1991-62434	19910305
PRIORITY APPLN. INFO.:			KR 1990-2811	19900305

AB Human insulin-like growth factor I (IGF-1) is manufactured in Escherichia coli as a fusion protein with β-galactosidase with the linking peptide containing a **cleavage site** for **enterokinase** or for hydroxylamine. A cDNA encoding IGF-1 was cloned from a liver cDNA bank by standard methods and cloned into pUC8 to give a chimeric gene for a β-galactosidase-IGF-1 fusion protein containing an **enterokinase cleavage site** under control of the tac promoter. Expression of the gene resulted in accumulation of the fusion protein in inclusion bodies. The inclusion bodies were solubilized in 8M urea and the fusion protein purified chromatog. After removal of urea the protein was resuspended in an **enterokinase** buffer after reduction of disulfide bonds with diethanol disulfide and IGF-1 recovered after cleavage with **enterokinase**.

Search completed by David Schreiber 308-4292

L22 ANSWER 43 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1989:19409 HCAPLUS
DOCUMENT NUMBER: 110:19409
TITLE: Bacterial expression vectors containing lipoprotein gene 5' sequences
INVENTOR(S): Mayne, Nancy G.; Burnett, J. Paul; Belegaje, Ramamoorthy; Hsiung, Hansen M.
PATENT ASSIGNEE(S): Lilly, Eli, and Co., USA
SOURCE: U.S., 21 pp. Cont.-in-part of U.S. Ser. No. 381,992, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4745069	A	19880517	US 1984-586581	19840306
HU 31783	O	19840528	HU 1983-1810	19830523
HU 197349	B	19890328		

PRIORITY APPLN. INFO.: US 1982-381992 19820525

AB A plasmid for efficient expression of exogenous genes comprises the 5' untranslated region and promoter of the lipoprotein (lpp) gene operably linked to a translation start codon, a sequence encoding an **enterokinase cleavage site**, and the gene for the exogenous protein, as well as a replicon and ≥1 genes for selectable markers. Plasmid pCC101, containing the Escherichia coli lpp gene 5' untranslated sequence and promoter and a gene encoding an **enterokinase** cleavage peptide fused to bovine growth hormone, was constructed. Fusion protein 240 mg was obtained from 22 g E. coli transformed with the plasmid. The biol. activity of the growth hormone released by **enterokinase** cleavage was comparable to that of a bovine growth hormone obtained from the National Pituitary Agency (as measured by proximal tibia epiphyseal cartilage growth in hypophysectomized female rats).

L22 ANSWER 44 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1987:28521 HCAPLUS
DOCUMENT NUMBER: 106:28521
TITLE: Improved expression using fused genes providing for protein product
INVENTOR(S): Cousens, Lawrence S.; Tekamp-Olson, Patricia A.; Shuster, Jeffrey R.; Merryweather, James P.
PATENT ASSIGNEE(S): Chiron Corp., USA
SOURCE: Eur. Pat. Appl., 36 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 196056	A2	19861001	EP 1986-104066	19860325
EP 196056	A3	19871223		
EP 196056	B1	19910522		

R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE

Search completed by David Schreiber 308-4292

CA 1260858	A1	19890926	CA 1986-504984	19860325
AT 63757	E	19910615	AT 1986-104066	19860325
DK 8601421	A	19860929	DK 1986-1421	19860326
JP 61268193	A2	19861127	JP 1986-70648	19860328
JP 08029096	B4	19960327		
US 4751180	A	19880614	US 1986-845737	19860328
JP 06014793	A2	19940125	JP 1993-40008	19930301
JP 2545686	B2	19961023		
US 2002028481	A1	20020307	US 1995-449070	19950524
US 2002146764	A1	20021010	US 2001-931216	20010816

PRIORITY APPLN. INFO.:

US 1985-717209 A 19850328
EP 1986-104066 A 19860325
US 1986-845737 A3 19860328
US 1988-169833 B1 19880317
US 1991-680046 A2 19910329
US 1993-88566 B1 19930706
US 1995-449070 B1 19950524

AB A method for enhancing the production of heterologous proteins in fungi by recombinant DNA techniques involves fusion of a gene encoding a heterologous protein produced in large amount and in stable form in the host to a sequence encoding a desired heterologous protein, where the hybrid proteins produced are joined by a selectively cleavable linkage. Plasmid pYASI1 was constructed which contains the human superoxide dismutase gene fused to the amino terminus of the human proinsulin gene, with a methionine codon at the junction, under the control of the hybrid inducible ADH2-GAP promoter and the GAP terminator. The fusion protein produced by yeast transformants accounts for ≥10% of the total cell protein. After cleavage of the hybrid protein at the methionine junction using CNBr and formic acid in water, the proinsulin was converted to its S-sulfonate form in the presence of urea, Na sulfite, and Na tetrathionate, and was purified on an ion-exchange column. Proinsulin-S-sulfonate obtained was 90% pure, and the yield was 150 mg protein/124 g yeast.

L22 ANSWER 45 OF 45 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1984:133583 HCAPLUS
DOCUMENT NUMBER: 100:133583
TITLE: Cloning vectors for expression of exogenous protein
INVENTOR(S): Mayne, Nancy Gail; Burnett, James Paul, Jr.; Belegaje, Ramamoorthy; Hsiung, Hansen Maxwell
PATENT ASSIGNEE(S): Lilly, Eli, and Co. , USA
SOURCE: Eur. Pat. Appl., 61 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 95361	A1	19831130	EP 1983-302935	19830523
EP 95361	B1	19890726		
R: BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
IL 68753	A1	19890131	IL 1983-68753	19830522
GB 2121054	A1	19831214	GB 1983-14183	19830523
GB 2121054	B2	19860226		
DK 8302306	A	19831126	DK 1983-2306	19830524
AU 8314912	A1	19831201	AU 1983-14912	19830524
AU 560965	B2	19870430		

Search completed by David Schreiber 308-4292

JP 58219199	A2	19831220	JP 1983-92197	19830524
JP 07059193	B4	19950628		
DD 210306	A5	19840606	DD 1983-251214	19830524
CA 1231068	A1	19880105	CA 1983-428700	19830524
JP 06073096	A2	19940315	JP 1992-351893	19920917

PRIORITY APPLN. INFO.: US 1982-381992 19820525
US 1982-382051 19820525

AB A recombinant DNA cloning vector is constructed by ligating (a) a replication origin, (b) a selection marker gene (gene for ampicillin resistance), (c) and an in-tandem DNA sequence comprising a promoter for a lipoprotein control sequence, the 5' untranslated region of a lipoprotein expression-control sequence (lpp gene from a gram-neg. bacterium), and a start codon that is followed immediately by a sequence coding for an exogenous protein or by a sequence coding for an **enterokinase** [89382-91-2] **cleavage site** to which is immediately joined a sequence coding for an exogenous protein. When used as a cloning vector the lpp sequences control expression of exogenous DNA, but a nonhybrid protein product is formed; i.e. the translation product comprises methionine-optionally an **enterokinase cleavage site**-exogenous protein. Treatment with **enterokinase** removes the methionyl residue and leaves mature exogenous protein. Thus, to a plasmid containing the Escherichia coli lipoprotein expression control sequence and plasmid pBR322 ampicillin-resistance genes was ligated a human growth hormone [12629-01-5] coding region with the use of a synthetic double-stranded DNA fragment complementary at 1 end to the natural lpp gene sequence (from the tbaI site through the initiating methionine codon), and at the other end, to the 1st 47 nucleotides of the gene for human growth hormone. The plasmid obtained, pNM645, was cloned in E. coli, and methionyl human growth hormone [82030-87-3] expression was verified by radioimmunoassay. The protein transcript represented 40% of the total protein with a yield of ≥2 million mols./cell. Biol. activity of the methionyl growth hormone with respect to proximal epiphyseal cartilage width in hypophysectomized female rats was the same as that of human growth hormone from cadavers.